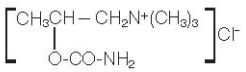
BETHANECHOL CHLORIDE - bethanechol chloride tablet
Abrika Pharmaceuticals LLLP

DESCRIPTION

Bethanechol chloride, a cholinergic agent, is a synthetic ester which is structurally and pharmacologically related to acetylcholine. Its chemical name is 2-[(aminocarbonyl) oxy]-N,N,N-trimethyl-1-propanaminium chloride. Bethanechol chloride is a white, hygroscopic, crystalline powder having a slight amine-like odor and is freely soluble in water. The structural formula is:



Molecular weight: 196.68
Molecular formula: $C_7H_{17}ClN_2O_2$
Bethanechol chloride is available as 10 mg, 25 mg, and 50 mg scored tablets intended for oral use.
Inactive Ingredients: Each tablet contains calcium pyrophosphate, magnesium stearate, microcrystalline cellulose, and corn starch. Additionally, the 50 mg strength contains: FD&C Blue No. 2 Aluminum Lake and FD&C Yellow No. 6 Aluminum Lake.

CLINICAL PHARMACOLOGY

Bethanechol chloride acts principally by producing the effects of stimulation of the parasympathetic nervous system. It increases the tone of the detrusor urinae muscle, usually producing a contraction sufficiently strong to initiate micturition and empty the bladder. It stimulates gastric motility, increases gastric tone, and often restores impaired rhythmic peristalsis.
Stimulation of the parasympathetic nervous system releases acetylcholine at the nerve endings. When spontaneous stimulation is reduced and therapeutic intervention is required, acetylcholine can be given, but is rapidly hydrolyzed by cholinesterase, and its effects are transient. Bethanechol chloride is not destroyed by cholinesterase and its effects are more prolonged than those of acetylcholine.
Effects on the G.I. and urinary tract sometimes appear within 30 minutes after oral administration of bethanechol chloride, but more often 60-90 minutes are required to reach maximum effectiveness. Following oral administration, the usual duration of action of bethanechol is one hour, although large doses (300-400 mg) have been reported to produce effects for up to six hours. Subcutaneous injection produces a more intense action on bladder muscle than does oral administration of the drug.
Because of the selective action of bethanechol, nicotinic symptoms of cholinergic stimulation are usually absent or minimal when orally or subcutaneously administered in therapeutic doses, while muscarinic effects are prominent. Muscarinic effects usually occur within 5-15 minutes after subcutaneous injection, reach a maximum in 15-30 minutes, and disappear within two hours. Doses that stimulate micturition and defecation and increase peristalsis do not ordinarily stimulate ganglia or voluntary muscles. Therapeutic test doses in normal human subjects have little effect on heart rate, blood pressure, or peripheral circulation.
Bethanechol chloride does not cross the bloodbrain barrier because of its charged quaternary amine moiety. The metabolic fate and mode of excretion of the drug have not been elucidated.

A clinical study[1] was conducted on the relative effectiveness of oral and subcutaneous doses of bethanechol chloride on the stretch response of bladder muscle in patients with urinary retention. Results showed that 5 mg of the drug given subcutaneously stimulated a response that was more rapid in onset and of a larger magnitude than an oral dose of 50 mg, 100 mg, or 200 mg. All the oral doses, however, had a longer duration of effect than the subcutaneous dose. Although the 50 mg oral dose caused little change in intravesical pressure in this study, this dose has been found in other studies to be clinically effective in the rehabilitation of patients with decompensated bladders.

1Diokno AC, Lapides J: Urology 10:23-24 (July) 1977

INDICATIONS AND USAGE

Bethanechol chloride is indicated for the treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention, and neurogenic atony of the urinary bladder with retention.

CONTRAINDICATIONS

Bethanechol chloride is contraindicated in individuals with hypersensitivity to bethanechol chloride tablets, hyperthyroidism, peptic ulcer, latent or active bronchial asthma, pronounced bradycardia or hypotension, vasomotor instability, coronary artery disease, epilepsy, and parkinsonism.
Bethanechol chloride should not be employed when the strength or integrity of the gastrointestinal or bladder wall is in question, or in the presence of mechanical obstruction; when increased muscular activity of the gastrointestinal tract or urinary bladder might prove harmful, as following recent urinary bladder surgery, gastrointestinal resection and anastomosis, or when there is possible gastrointestinal obstruction; in bladder neck obstruction, spastic gastrointestinal disturbances, acute inflammatory lesions of the gastrointestinal tract, or peritonitis; or in marked vagotonia.

PRECAUTIONS

General
In urinary retention, if the sphincter fails to relax as bethanechol contracts the bladder, urine may be forced up the ureter into the kidney pelvis. If there is bacteriuria, this may cause a reflux infection.

Information for Patients
Bethanechol chloride tablets should preferably be taken one hour before or two hours after meals to avoid nausea or vomiting. Dizziness, light-headedness or fainting may occur, especially when getting up from a lying or sitting position.

Drug Interactions
Special care is required if this drug is given to patients receiving ganglion blocking compounds, because a critical fall in blood pressure may occur. Usually, severe abdominal symptoms appear before there is such a fall in the blood pressure.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate the effects upon fertility, mutagenic, or carcinogenic potential of bethanechol chloride.

Pregnancy

Teratogenic Effects
Pregnancy Category C. Animal reproduction studies have not been conducted with bethanechol chloride. It is also not known whether bethanechol chloride can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Bethanechol chloride should be given to a pregnant woman only if clearly needed.

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions from bethanechol chloride in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS
Adverse reactions are rare following oral administration of bethanechol chloride, but are more common following subcutaneous injection. Adverse reactions are more likely to occur when dosage is increased. The following adverse reactions have been observed:
Body as a Whole: Malaise.
Cardiovascular: Fall in blood pressure with reflex tachycardia, vasomotor response.
Digestive: Colicky pain, abdominal cramps or discomfort, diarrhea, nausea and belching, salivation, and borborygmi.
Skin: Flushing, producing a feeling of warmth; sensation of heat about the face; sweating.
Respiratory: Asthmatic attacks and bronchial constriction.
Nervous System: Headache.
Renal: Urinary urgency.
Special Senses: Lacrimation, miosis.
Causal Relationship Unknown: The following adverse reactions have been reported, and a causal relationship to therapy with bethanechol chloride has not been established:
Body as a Whole: Malaise.
Nervous System: Seizures.

OVERDOSAGE
Early signs of overdosage are abdominal discomfort, salivation, flushing of the skin (“hot feeling”), sweating, nausea and vomiting. *Atropine sulfate is a specific antidote*. The recommended dose for adults is 0.6 mg. Repeat doses can be given every two hours, according to clinical response. The recommended dosage in infants and children up to 12 years of age is 0.01 mg/kg (to a maximum single dose of 0.4 mg), repeated every two hours as needed until the desired effect is obtained, or adverse effects of atropine preclude further usage. Subcutaneous injection of atropine is preferred, except in emergencies when the intravenous route may be employed. The oral LD_{50} of bethanechol chloride is 1510 mg/kg in the mouse.

DOSAGE AND ADMINISTRATION
Dosage must be individualized, depending on type and severity of the condition to be treated.
Preferably, give the drug when the stomach is empty. If taken soon after eating, nausea and vomiting may occur.

The usual adult oral dose ranges from 10 to 50 mg three or four times a day. The minimum effective dose is determined by giving 5 to 10 mg initially, and repeating the same amount at hourly intervals until satisfactory response occurs, or until a maximum of 50 mg has been given. The effects of the drug sometimes appear within 30 minutes, and are usually maximal within 60 to 90 minutes. The drugs effects persist for about one hour.
If necessary, the effects of the drug can be abolished promptly by atropine (see OVERDOSAGE).

HOW SUPPLIED
Bethanechol Chloride Tablets, USP is available as follows:
10 mg: white, scored tablet, coded “WPC 004” on scored side and“DUVOID 10” on smooth side. NDC 67767-144-01: bottle of 100
25 mg: white, scored tablet, coded “WPC 005” on scored side and“DUVOID 25” on smooth side. NDC 67767-145-01: bottle of 100
50 mg: tan, scored tablet, coded “WPC 006” on scored side and “DUVOID 50” on smooth side. NDC 67767-146-01: bottle of 100
Dispense in a tight container as defined in the USP.
Store at 25ºC (77ºF); excursions permitted to 15º-30ºC (59º-86ºF) [See USP Controlled Room Temperature].
Keep this and all medication out of the reach of children.

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